REMARKS

Claims 1-19 are pending.

Claims 7-15, 18, and 19 have been withdrawn from consideration.

By this Amendment, claim 3 has been amended to recite "peaks at 5.3 ±0.2 and 8.3 ±0.2 degrees 2θ." Claim 17 has been similarly amended. Support for these amendments is found in the specification at page 5, lines 14-15.

The Applicants thank the Examiner for indicating that claim 2 is allowed.

Claim objections

Claims 1, 3-6, 16, and 17 were objected to as being substantial duplicates of claim 2.

M.P.E.P. §706.03(k) states that "mere difference in scope between claims has been held to be enough" to prevent claims from being considered substantial duplicates. Here all of claims 1, 3-6, 16, and 17 differ in scope from claim 2. Claim 2 is directed to a crystalline form of atorvastatin that must have an X-ray powder diffractogram substantially as that of the diffractogram depicted in claim 2. In contrast, none of claims 1, 3-6, 16, and 17 require that the crystalline forms claimed have the diffractogram depicted in claim 2. This alone provides for a difference in scope between claim 2 and each of claims 1, 3-6, 16, and 17 and leads to the conclusion that an objection of claims 1, 3-6, 16, and 17 as being substantial duplicates of claim 2 is improper.

Court decisions have upheld an applicant's right to claim an invention in a reasonable number of ways. *See In re Flint*, 411 F.2d 1353, 1357 (C.C.P.A. 1969) ("applicants should be allowed reasonable latitude in stating their claims in regard to

number and phraseology employed."); *In re Chandler*, 319 F.2d 211, 225 ("[t]he right of applicants to freedom of choice in selecting phraseology which truly points out and defines their inventions should not be abridged."). In order to support the present objection, the Office Action must "set forth typical examples of substantial duplication or lack of material differentiation, discuss[ed] the relative complexity of the invention, allege[d] a lack of difference in scope of the claims, and refer[red] to representative prior art." *In re Flint*, 411 F.2d at 1356-1357.

The Office Action has done none of this. There has been no analysis along the lines required by *In re Flint*. There has been no analysis to demonstrate that the number of ways the Applicants have claimed their invention is unreasonable or that the claims objected to are of the same scope as allowed claim 2. The entirety of the Office Action directed to this objection reads as follows:

> Claims 1, 3-6, 16 and 17 are objected to for being substantial duplicate [sic] of claim 2. When two claims in an application are duplicates, or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to reject the other as being a substantial duplicate of the allowed claim.

Office Action, page 3, lines 8-15.

Thus, there is no reasoned analysis at all in support of this objection.

In view of the above, it is respectfully requested that this objection be withdrawn.

The rejection under 35 U.S.C. §112

Claims 1, 3, 6, 16, and 17 were rejected for lack of written description.

Claims 3 and 17 have been amended to recite "5.3 ±0.2 and 8.3 ±0.2 degrees 2θ." Accordingly, it is respectfully requested that this rejection be withdrawn.

Claim 16 was rejected for lack of enablement.

This rejection relies on two premises: (1) metabstable crystalline forms tend to convert to the most stable form; and (2) the usual procedures used to prepare pharmaceutical compositions (grinding, milling, adding excipients, etc.) will convert a metastable form to a stable form.

The Applicants traverse this rejection because no evidence supporting the second premise has been provided.

The only evidence cited in support of this rejection is Rouhi Chemical and Engineering News, February 24, 2003, pages 32-35. Rouhi at most shows that metastable forms tend to, i.e., may possibly, convert to the most thermodynamically stable form. See the Office Action, page 7, lines 2-5: "Polymorphs tend to convert from less stable to more stable forms (Rouhi, Chemical and Engineering News, February 24, 2003, pages 32-35, especially page 32)."

The specification teaches that Form V can be formulated into pharmaceutical compositions. See page 10, line 19 to page 13, line 3. Thus, the specification teaches that Form V will persist after being formulated into pharmaceutical compositions. The burden is on the USPTO to provide evidence or reasoning, not just mere speculation, as to why this teaching of the specification is incorrect. See *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1971), where the United States Court of Customs and Patent Appeals stated:

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein .... [emphasis in original]
>
> 439 F.2d at 223, 169 U.S.P.Q. at 369.

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. [italics in original; underscoring added]
>
> 439 F.2d at 224, 169 U.S.P.Q. at 370.

The Office Action has not met this burden. A premise of this rejection is that Form V will not persist upon being formulated into a pharmaceutical composition. This goes far beyond the evidence that the Office Action has cited in support of this rejection. The cited evidence (Rouhi) at most shows that metastable forms may possibly convert to the most thermodynamically stable form. The cited evidence says nothing about the likelihood, the speed of, or the completeness of, such a conversion.

There is nothing in Rouhi that supports the proposition that Form V is likely to convert so rapidly and so completely into the most stable form when formulated into a pharmaceutical composition that a person skilled in the art could not practice the invention defined in claim 16. Nor was any other evidence provided to support such a proposition.

The only reason given in the Office Action for such a proposition is the speculation that if Form V is subjected to the usual procedures for making pharmaceutical compositions it will convert to other forms. See, e.g., the Office Action, page 6, line 13 to page 7, line 2:

> The preparation of he pharmaceutical compositions requires creating solutions, milling, adding diluents, excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline from, if in the metastable state, to resort back to the most thermodynamically stable form, which is the form with the lowest vapor pressure. [underscoring added]

The key portion of the above passage is the underlined quote. This quote expresses the second premise underlying this rejection. The Office Action provided no evidence in support of this quote.

Furthermore, Rouhi teaches that the second premise underlying this rejection is wrong. Rouhi teaches that the likely outcome of formulation of a crystalline form, when carried out by those skilled in the art, is that the crystalline form used would maintain itself for a reasonable period of time such that the pharmaceutical composition would be useful. This is implicit in Rouhi since one of the main themes in Rouhi is that pharmaceutical companies are actively seeking new crystalline forms of compounds (even metastable forms) in order to formulate these crystalline forms into pharmaceutical compositions (see page 32, right column; "[M]uch effort is being expended looking for metastable forms of currently marketed drugs whose stable forms have been around for a long time." It would make no sense for pharmaceutical companies to behave in such a manner if the second premise underlying this rejection were correct.

Furthermore, conversion to the most stable form can be quite slow and less stable crystalline forms can co-exist with the most stable crystalline form. See U.S. Pharmacopia #23, National Formulary #18 (1995), page 1843, entry (941), X-Ray Diffraction[1]:

> Many compounds are capable of crystallizing in more than one type of crystal lattice. At any particular temperature and pressure, only one crystalline form (polymorph) is thermodynamically stable. Since the rate of phase transformation of a metastable polymorph to the stable one can be quite slow, it is not uncommon to find several polymorphs of crystalline pharmaceutical compounds existing under normal handling conditions.

[1] A copy of this reference was provided with the Information Disclosure Statement that was filed on February 16, 2006..

The quotation above shows that the second premise underlying this rejection ignores the fact that, even if conversion to a more stable form occurs, that conversion may be "quite slow." In fact, this quotation implies that such "quite slow" conversion is "not uncommon." Thus, the evidence of record indicates that the likely outcome of formulating Form F into pharmaceutical compositions is that Form F will persist, at least for a period of time sufficient to provide a useful pharmaceutical composition.

In view of the above, it can be seen that the evidence provided in the Office Action is inadequate to support this rejection. Thus, the Office Action failed to provide "acceptable evidence or reasoning" to support the rejection, as required by *Marzocchi.*

The Office Action reads claim 16 as including solutions of Form V where the pharmaceutically acceptable carrier is water. See the Office Action, page 7, lines 9-14. The Applicants note that claim 16 is directed to a pharmaceutical composition "that is a solid or suspension." In view of this, it is respectfully requested that this aspect of the rejection is improper. Thus, the Office Action's reading of claim 16 is incorrect.

The Applicants believe that the above discussion demonstrates that claim 16 does not lack enablement. In view of the above, it is respectfully requested that this rejection be withdrawn.

Claims 1, 3, 6, 16, and 17 were rejected for indefiniteness.

This rejection is based on the premise that claims 1, 3, 6, 16, and 17 are substantial duplicates of claim 2. As discussed above, this is incorrect. Accordingly, it is respectfully requested that this rejection be withdrawn.

The rejection under 35 U.S.C. §102(b)

Claim 16 was rejected as being anticipated by International Patent Publications WO 97/03959 (Briggs) or WO 97/03958 (McKenzie).

The Office Action stated that Briggs disclosed Form II atorvastatin, which has X-ray powder diffraction patterns and ^{13}C NMR chemical shifts "embraced by the instant claimed invention (see especially instant claims 3 and 5)." (Office Action, page 13, lines 1-2).

Claim 16 depends from claim 1, 3, or 5. Thus, if Briggs does not anticipate claim 1, 3, or 5, Briggs does not anticipate claim 16.

Claim 3 has been amended to require a PXRD peak at 5.3 ±0.2 degrees 2θ (i.e., between 5.1-5.5 degrees 2θ), a PXRD peak at 8.3 ±0.2 degrees 2θ (i.e., between 8.1-8.5 degrees 2θ), and a broad peak at 18-23 ±0.2 degrees 2θ with a maximum at 18.3 ±0.2 degrees 2θ (i.e., a broad peak between 17.8-23.2 degrees 2θ with a maximum at 18.1-18.5 degrees 2θ).

Form II of Briggs does not meet these limitations of amended claim 3 because Form II does not have a peak between 5.1-5.5 degrees 2θ or a peak between 8.1-8.5 degrees 2θ. Form II also does not have a broad peak between 17.8-23.2 degrees 2θ with a maximum at 18.1-18.5 degrees 2θ. See the table on page 6 of Briggs (reproduced below), which shows the PXRD peaks of Form II.

2θ	d	Relative Intensity (>20%) Ground 2 Minutes
5.582	15.8180	42.00
7.384	11.9620	38.63
8.533	10.3534	100.00
9.040	9.7741	92.06
12.440 (broad)	7.1094	30.69
15.771 (broad)	5.6146	38.78
17.120-17.360 (broad)	5.1750-5.1040	63.66-55.11
19.490	4.5507	56.64
20.502	4.3283	67.20
22.706-23.159 (broad)	3.9129-3.8375	49.20-48.00
25.697 (broad)	3.4639	38.93
29.504	3.0250	37.86

Thus, Briggs does not anticipate claim 3.

Claim 1 depends from claim 3. Thus, Briggs does not anticipate claim 1.

Claim 5 requires a ^{13}C NMR spectrum characterized by signals at 21.9, 25.9, 118.9, 122.5, 128.7, 161.0 and 167.1 ppm.

Form II of Briggs does not meet these limitations of claim 5 because Form II does not have any of these signals, with the exception of the signal at 161.0 ppm. See the table on page 7 of Briggs (reproduced below), showing the ^{13}C NMR signals of Form II.

Assignment	Chemical Shift
Spinning Side Band	209.1
Spinning Side Band	206.8
C12 or C25	181 (broad)
C12 or C25	163 (broad)
C16	161 (broad)
Aromatic Carbons	
C2-C5, C13-C18, C19-C24, C27-C32	140.5
	134.8
	133.3
	129.0
	122.9
	121.4
	120.3
	119.0
	117.1
	115.7
	114.7
C8, C10	70.6
	69.0
	68.0
	67.3
Spinning Side Band	49.4
Spinning Side Band	48.9
Methylene Carbons	
C6, C7, C9, C11	43.4
	42.3
	41.7
	40.2
C33	27.5
C34	22.8 (broad)

Thus, Briggs does not anticipate claim 5.

Since Briggs does not anticipate any of claims 1, 3, or 5, Briggs does not anticipate claim 16.

The Office Action stated that McKenzie disclosed Form III atorvastatin, which has X-ray powder diffraction patterns and ^{13}C NMR chemical shifts "embraced by the instant claimed invention (see especially instant claims 3 and 5)." (Office Action, page 13, lines 6-7).

Claim 3 has been amended to require a PXRD peak at 5.3 ±0.2 degrees 2θ (i.e., between 5.1-5.5 degrees 2θ), a PXRD peak at 8.3 ±0.2 degrees 2θ (i.e., between 8.1-8.5 degrees 2θ), and a broad peak at 18-23 ±0.2 degrees 2θ with a maximum at

18.3 ±0.2 degrees 2θ (i.e., a broad peak between 17.8-23.2 degrees 2θ with a maximum at 18.1-18.5 degrees 2θ).

Form III of McKenzie does not meet these limitations of amended claim 3 because Form III does not have a peak between 5.1-5.5 degrees 2θ. See the table on page 4 of McKenzie (reproduced below), showing the PXRD peaks of Form III.

2θ	d	Relative Intensity (>25%)
4.123	21.4140	49.20
4.993	17.6832	30.82
5.768	15.3099	28.69
7.670	11.5173	25.49
8.451	10.4538	100.00
15.962	5.5478	32.59
16.619	5.3298	62.34
17.731	4.9981	49.29
18.267	4.8526	45.12
18.870	4.6989	39.52
19.480	4.5531	36.59
19.984	4.4393	70.34
20.294	4.3722	69.54
21.105	4.2061	37.39
21.670	4.0976	36.50
23.318	3.8117	38.63
24.405	3.6442	65.54
24.967	3.5635	27.20
25.397	3.5041	33.75

Thus, McKenzie does not anticipate claim 3.

Claim 1 depends from claim 3. Thus, McKenzie does not anticipate claim 1.

Claim 5 requires a ^{13}C NMR spectrum characterized by signals at 21.9, 25.9, 118.9, 122.5, 128.7, 161.0 and 167.1 ppm.

Form III of McKenzie does not meet these limitations of claim 5 because Form III does not have any of these signals, with the exception of the signal at 161.0

ppm. See the table on page 5 of McKenzie (reproduced below), showing the ^{13}C NMR signals of Form III.

Assignment	Chemical Shift
Spinning Side Band	214.8
	209.3
	202.3
C12 or C25	184.9
C12 or C25	166.7
C16	161.0(weak, broad)
Aromatic Carbons	
C2-C5, C13-C18, C19-C24, C27-C32	140.1
	135.2
	131.8
	128.9
	124.3
	122.2
	117.2
	114.9
C8, C10	69.8
	67.3
	65.6
Methylene Carbons	
C6, C7, C9, C11	44.1
	40.4
	35.4
C33	27.0
	24.1
C34	22.1
	19.9

Thus, McKenzie does not anticipate claim 5.

Claim 16 depends from claim 1, claim 3, or claim 5. Since McKenzie does not anticipate claim 1, claim 3, or claim 5, McKenzie also does not anticipate claim 16.

In view of the above, it is respectfully requested that these anticipation rejections be withdrawn.

Withdrawn claims

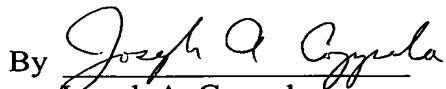
The Applicants respectfully request rejoinder of the withdrawn claims.

Claims 7-15, 18, and 19 are process claims that depend from product claims 2-5. As discussed above, claims 2-5 are allowable. Therefore, rejoinder is proper.

The time for responding to the Office Action was set for August 4, 2006. Enclosed is a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this response.

The Applicants hereby make a Conditional Petition for any relief available to correct any defect seen in connection with this filing, or any defect seen to be remaining in this application after this filing. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully submitted,

By 
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